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10/701,152	11/04/2003	Brian Horsburgh	08582/007003	5512
21559	7590	12/28/2004	EXAMINER	
CLARK & ELBING LLP			GUZO, DAVID	
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BOSTON, MA 02110			PAPER NUMBER	

1636

DATE MAILED: 12/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/701,152

Applicant(s)

HORSBURGH ET AL.

Examiner

David Guzo

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 29 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 04 November 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 3/18/04.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### Detailed Action

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-4, 7, 9, 11, 13 and 15 are rejected under 35 U.S.C. 102(a) as being anticipated by Messerle et al.

Both Messerle et al. (Cited by applicants, PNAS, Dec. 1997, Vol. 94, pp. 14759-14763, see whole article, particularly the Abstract; Fig. 1, p. 14760, right column and p. 14761) and applicants recite a BAC comprising a nucleic acid sequence that directs formation of a recombinant lytic or non-lytic virus (i.e. the herpes virus CMV or mutants thereof), which contains heterologous nucleic acid sequences (i.e. lacZ insertion), upon introduction into a cell. Messerle et al. also recites introducing the BAC-viral constructs into cells and subsequent viral induced lysis of said cells. It is noted that murine CMV can be a lytic or non-lytic virus depending on the cell type or cell line or tissue or animal infected. Therefore, Messerle et al. teaches the claimed invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States

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only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4, 7, 9 and 13 rejected under 35 U.S.C. 102(e) as being anticipated by Ketner et al.

Applicants claim an artificial chromosome construct (which can be a YAC) which comprises a nucleic acid sequence that directs formation of a recombinant virus (which can be a lytic or non-lytic virus and can be a herpes virus and optionally can contain a heterologous gene which can be therapeutic or a vaccine antigen) upon introduction into a cell.

Ketner et al. (Cited by applicants, U.S. Patent 5,776,745, issued 7/7/98, priority to 7/23/93, see whole document, particularly column 1, lines 57-67; column 2, lines 1-25; column 4, lines 4-17; column 6, lines 62-67; column 7, lines 1-26 and Example 3) recites a yeast artificial chromosome (YAC) which can comprise a nucleic acid sequence that directs formation of a recombinant virus which can be lytic or non-lytic (i.e. any RNA virus or any DNA virus such as a herpes virus or adenovirus) wherein the virus can optionally contain a heterologous nucleic acid sequence (i.e. CYH2 that confers sensitivity to cycloheximide) and methods of introducing heterologous nucleic acids into target cells comprising introducing the YACs into said cells. Ketner et al. therefore teaches the claimed invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 19 is rejected under 35 U.S.C. 102(b) as being anticipated by Pachnis et al.

Applicants claim a cell comprising an artificial chromosome construct stably integrated into its genome.

Pachnis et al. (PNAS, 1990, Vol. 87, pp. 5109-5113, see whole article, particularly the Abstract and pp. 5112-5113) recites mouse L cells comprising a YAC stably integrated into the genome of said cells. Pachnis et al. therefore teaches the claimed invention.

Claims 1-2, 4, 8, 11 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Luckow et al.

Applicants and Luckow et al. (J. Virol., 1993, Vol. 67, No. 8, pp. 4566-4579, see whole article, particularly the Abstract, Fig. 1, pp. 4568-4569, paragraph bridging pp. 4572-4573, p. 4574) recite an artificial chromosome construct (a F factor based bacterial artificial chromosome) comprising a recombinant baculovirus genome containing a heterologous nucleic acid sequence. Introduction of the bacterial artificial chromosome into insect cells results in expression of the heterologous sequence, replication of the virus and lysis of the cells. It is noted that the bacterial artificial chromosomes disclosed by Luckow et al. are based upon the well studied *E. coli* F factor (a mini-F replicon) wherein said F factor is capable of controlled expression in *E.*

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*coli* and capable of maintaining and carrying large fragments of DNA. Luckow et al. therefore teaches the claimed invention.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 5, 6 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ketner et al. in view of Kaplitt et al.

Applicants claim an artificial chromosome construct comprising a nucleic acid sequence that directs formation of a recombinant herpes simplex virus (HSV).

Ketner et al. is applied as in the above 35 USC 102(e) rejection. Ketner et al. specifically recites that one of the viruses that may be propagated in YACs is a herpes virus. Ketner et al. also recites that their invention will facilitate the production of

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recombinant viral vectors for use in gene therapy (see paragraph bridging columns 1-2).

Ketner et al. does not explicitly recite the generation of a YAC comprising a HSV

genome or generation of artificial chromosomes comprising recombinant viruses

encoding therapeutic genes such as enzymes, growth factors, etc..

Kaplitt et al. (J. Neuroscience Methods, January 1997, Vol. 71, pp. 125-132, see whole article, particularly the Abstract, pages 126-128) recites the extensive literature on the generation and use of recombinant HSV vectors to deliver therapeutic genes (i.e. tyrosine kinase, glucose transporter, bcl-2) to the neural cells.

The ordinary skilled artisan, seeking to choose a specific recombinant herpesvirus for insertion into an artificial chromosome (as taught by Ketner et al.) would have been motivated to choose HSV because Kaplitt et al. recites that HSV has been the herpesvirus which has been extensively studied and adapted to express therapeutic genes in human neural cells. It would have been obvious for the ordinary skilled artisan to generate an artificial chromosome comprising a HSV genome because Ketner et al. specifically recites that herpesviruses are contemplated as viruses to be propagated using artificial chromosomes and Kaplitt et al. indicates that HSV is well characterized and has been the subject of extensive research as a gene therapy agent for delivery of therapeutic genes to neural cells. With regard to claims 5-6, it is noted that these claims are not limited to HSV; however, the disclosure of Kaplitt et al. with regard to generation of HSV (and other recombinant viral vectors which express therapeutic genes) renders these claims obvious since they are generic with regard to the recombinant viruses included in the artificial chromosomes. Given the teachings of the cited references and

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the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 5-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ketner et al. in view of Hanania et al.

Ketner et al. is recited as in the above 35 USC 102(e) and 103(a) rejections. Ketner et al. does not recite the generation of artificial chromosomes comprising a recombinant viral genome containing a therapeutic gene such as a growth factor, antisense sequence, enzyme, etc.

Hanania et al. (Am. J. Med., 1995, Vol. 99, pp. 537-552, see whole article, particularly Tables II and IV-V, pp. 541-543) recites the generation of recombinant viral vectors such as adenoviruses and herpesviral vectors for expression of therapeutic genes such as hormones, antisense sequences, enzymes, vaccine antigens, etc.

The ordinary skilled artisan, seeking to choose recombinant viruses for insertion into an artificial chromosome (as taught by Ketner et al.) would have been motivated to choose recombinant viruses capable of expressing therapeutic genes such as enzymes, hormones, antisense sequences, etc. because Hanania et al. recites that recombinant viral vectors such as adenoviruses and herpesviruses have been extensively studied and adapted to express therapeutic genes in human cells. It would have been obvious for the ordinary skilled artisan to generate an artificial chromosome comprising a recombinant viral genome capable of expressing a therapeutic gene because Ketner et

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al. specifically recites that the generation of YACs containing viral genomes can facilitate the generation of recombinant viral vectors for use in gene therapy. Given the teachings of the cited references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 11-18 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-8 of prior U.S. Patent No. 6,642,207. This is a double patenting rejection. The instant claims recite the same identical subject matter of the claims in the '207 patent.

Claim 8 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of prior U.S. Patent No. 6,277,621. This is a double patenting rejection. The instant claim recites the same identical subject matter as claim 1 in the '621 patent.

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The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-7, 9, 10 and 19-20 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S.

Patent No. 6,277,621. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are generic to all that is recited in claims 1-10 of the '621 patent. The subject matter of the '621 patent fall entirely within the scope of the instant claims. The claims of the '621 patent are limited to bacterial artificial chromosomes (BACs) comprising recombinant viruses while the claims of the instant application recite any artificial chromosomes comprising the same recombinant viruses. The claims in the '621 patent would therefore anticipate the instant claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 11, 12 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 (and dependent claims) are vague in the recitation, in claim 11, of the phrase "A method of producing a recombinant virus or in a cell" as it is unclear what applicants mean by this phrase. Possibly deletion of the word "or" would be remedial.

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

The Sequence Listing filed 4/29/04 is acceptable and has been entered.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571) 272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (571) 272-0781. The fax phone


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number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David Guzo  
December 13, 2004

  
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PRIMARY EXAMINER

  
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